```
attcggctcg agttcacctg gtgctgcttt gacttcaggc tcttccttct gcccagctcc      60
gtcccaccca gcagcccgca gagaaaggag gcagctggca ccacactggg ctttggagac     120
actgcgggga ctgtggaccc caccctgctg cacggagctc ctgcaaaagc aaacctgaga     180
accttgggtc ctcccagcgc ccagcc atg ggg gaa ctg tgc cgc agg gac tcc      233
                              Met Gly Glu Leu Cys Arg Arg Asp Ser
                               1               5

gca ctc acg gca ctg gac gag gag aca ctg tgg gag atg atg gag agc       281
Ala Leu Thr Ala Leu Asp Glu Glu Thr Leu Trp Glu Met Met Glu Ser
 10                  15                  20                  25

cac cgc cac agg atc gta cgc tgc atc tgc ccc agc cgc ctc acc ccc       329
His Arg His Arg Ile Val Arg Cys Ile Cys Pro Ser Arg Leu Thr Pro
                 30                  35                  40

tac ctg cgc cag gcc aag gtg ctg tgc cag ctg gac gag gag gag gtg       377
Tyr Leu Arg Gln Ala Lys Val Leu Cys Gln Leu Asp Glu Glu Glu Val
             45                  50                  55

ctg cac agc ccc cgg ctc acc aac agc gcc atg cgg gcc ggg cac ttg       425
Leu His Ser Pro Arg Leu Thr Asn Ser Ala Met Arg Ala Gly His Leu
         60                  65                  70

ctg gat ttg ctg aag act cga ggg aag aac ggg gcc atc gcc ttc ctg       473
Leu Asp Leu Leu Lys Thr Arg Gly Lys Asn Gly Ala Ile Ala Phe Leu
     75                  80                  85

gag agc ctg aag ttc cac aac cct gac gtc tac acc ctg gtc acc ggg -     521
Glu Ser Leu Lys Phe His Asn Pro Asp Val Tyr Thr Leu Val Thr Gly
 90                  95                 100                 105

ctg cag cct gat gtt gac ttc agt aac ttt agc ggt ctc atg gag aca       569
Leu Gln Pro Asp Val Asp Phe Ser Asn Phe Ser Gly Leu Met Glu Thr
                110                 115                 120

tcc aag ctg acc gag tgc ctg gct ggg gcc atc ggc agc ctg cag gag       617
Ser Lys Leu Thr Glu Cys Leu Ala Gly Ala Ile Gly Ser Leu Gln Glu
            125                 130                 135

gag ctg aac cag gaa aag ggg cag aag gag gtg ctg ctg cgg cgg tgc       665
Glu Leu Asn Gln Glu Lys Gly Gln Lys Glu Val Leu Leu Arg Arg Cys
        140                 145                 150

cag cag ctg cag gag cac ctg ggc ctg gcc gag acc cgt gcc gag ggc       713
Gln Gln Leu Gln Glu His Leu Gly Leu Ala Glu Thr Arg Ala Glu Gly
    155                 160                 165

ctg cac cag ctg gag gct gac cac agc cgc atg aag cgt gag gtt agc       761
Leu His Gln Leu Glu Ala Asp His Ser Arg Met Lys Arg Glu Val Ser
170                 175                 180                 185

gca cac ttc cat gag gtg ctg agg ctg aag gac gag atg ctc agc ctc       809
Ala His Phe His Glu Val Leu Arg Leu Lys Asp Glu Met Leu Ser Leu
                190                 195                 200
```

Fig. 1A

```
tcg ctg cac tat agc aat gcg ctg cag gag aag gag ctg gcc gcc tca      857
Ser Leu His Tyr Ser Asn Ala Leu Gln Glu Lys Glu Leu Ala Ala Ser
            205                 210                 215

cgc tgc cgc agc ctg cag gag gag ctg tat cta ctg aag cag gag ctg      905
Arg Cys Arg Ser Leu Gln Glu Glu Leu Tyr Leu Leu Lys Gln Glu Leu
        220                 225                 230

cag cga gcc aac atg gtt tcc tcc tgt gag ctg gaa ttg caa gag cag      953
Gln Arg Ala Asn Met Val Ser Ser Cys Glu Leu Glu Leu Gln Glu Gln
    235                 240                 245

tcc ctg agg aca gcc agc gac cag gag tcc ggg gat gag gag ctg aac     1001
Ser Leu Arg Thr Ala Ser Asp Gln Glu Ser Gly Asp Glu Glu Leu Asn
250                 255                 260                 265

cgc ctg aag gag gag aat gag aaa ctg cgc tcg ctg act ttc agc ctg     1049
Arg Leu Lys Glu Glu Asn Glu Lys Leu Arg Ser Leu Thr Phe Ser Leu
                270                 275                 280

gcg gag aag gac att ctg gag cag agc ctg gac gag gcg cgg ggg agc     1097
Ala Glu Lys Asp Ile Leu Glu Gln Ser Leu Asp Glu Ala Arg Gly Ser
            285                 290                 295

cga cag gag ctg gtg gag cgc atc cac tcg ctg cgg gag cgg gcc gtg     1145
Arg Gln Glu Leu Val Glu Arg Ile His Ser Leu Arg Glu Arg Ala Val
        300                 305                 310

gct gcc gag agg cag cga gag cag tac tgg gaa gag aag gaa cag acc     1193
Ala Ala Glu Arg Gln Arg Glu Gln Tyr Trp Glu Glu Lys Glu Gln Thr
    315                 320                 325

ctg ctg cag ttc cag aag agt aag atg gcc tgc caa ctc tac agg gag     1241
Leu Leu Gln Phe Gln Lys Ser Lys Met Ala Cys Gln Leu Tyr Arg Glu
330                 335                 340                 345

aag gtg aat gcg ctg cag gcc cag gtg tgc gag ctg cag aag gag cga     1289
Lys Val Asn Ala Leu Gln Ala Gln Val Cys Glu Leu Gln Lys Glu Arg
                350                 355                 360

gac cag gcg tac tcc gcg agg gac agt gct cag agg gag att tcc cag     1337
Asp Gln Ala Tyr Ser Ala Arg Asp Ser Ala Gln Arg Glu Ile Ser Gln
            365                 370                 375

agc ctg gtg gag aag gac tcc ctc cgc agg cag gtg ttc gag ctg acg     1385
Ser Leu Val Glu Lys Asp Ser Leu Arg Arg Gln Val Phe Glu Leu Thr
        380                 385                 390

gac cag gtc tgc gag ctg cgc aca cag ctt cgc cag ctg cag gca gag     1433
Asp Gln Val Cys Glu Leu Arg Thr Gln Leu Arg Gln Leu Gln Ala Glu
    395                 400                 405

cct ccg ggt gtg ctc aag cag gaa gcc agg acc agg gag ccc tgt cca     1481
Pro Pro Gly Val Leu Lys Gln Glu Ala Arg Thr Arg Glu Pro Cys Pro
410                 415                 420                 425
```

Fig. 1B

```
cgg gag aag cag cgg ctg gtg cgg atg cat gcc atc tgc ccc aga gac      1529
Arg Glu Lys Gln Arg Leu Val Arg Met His Ala Ile Cys Pro Arg Asp
                430                 435                 440

gac agc gac tgc agc ctc gtc agc tcc aca gag tct cag ctc ttg tcg      1577
Asp Ser Asp Cys Ser Leu Val Ser Ser Thr Glu Ser Gln Leu Leu Ser
            445                 450                 455

gac ctg agt gcc acg tcc agc cgc gag ctg gtg gac agc ttc cgc tcc      1625
Asp Leu Ser Ala Thr Ser Ser Arg Glu Leu Val Asp Ser Phe Arg Ser
        460                 465                 470

agc agc ccc gcg ccc ccc agc cag cag tcc ctg tac aag cgg gtg gcc      1673
Ser Ser Pro Ala Pro Pro Ser Gln Gln Ser Leu Tyr Lys Arg Val Ala
    475                 480                 485

gag gac ttc ggg gaa gaa ccc tgg tct ttc agc agc tgc ctg gag atc      1721
Glu Asp Phe Gly Glu Glu Pro Trp Ser Phe Ser Ser Cys Leu Glu Ile
490                 495                 500                 505

ccg gag gga gac ccg gga gcc ctg ccg gga gct aag gca ggc gac cca      1769
Pro Glu Gly Asp Pro Gly Ala Leu Pro Gly Ala Lys Ala Gly Asp Pro
                510                 515                 520

cac ctg gat tat gag ctc cta gac acg gca gac ctt ccg cag ctg gaa      1817
His Leu Asp Tyr Glu Leu Leu Asp Thr Ala Asp Leu Pro Gln Leu Glu
            525                 530                 535

agc agc ctg cag cca gtc tcc cct gga agg ctt gat gtc tcg gag agc      1865
Ser Ser Leu Gln Pro Val Ser Pro Gly Arg Leu Asp Val Ser Glu Ser
        540                 545                 550

ggc gtc ctc atg cgg cgg agg cca gcc cgc agg atc ctg agc cag gtc      1913
Gly Val Leu Met Arg Arg Arg Pro Ala Arg Arg Ile Leu Ser Gln Val
    555                 560                 565

acc atg ctg gcg ttc cag ggg gat gca ttg ctg gag cag atc agc gtc      1961
Thr Met Leu Ala Phe Gln Gly Asp Ala Leu Leu Glu Gln Ile Ser Val
570                 575                 580                 585

atc ggc ggg aac ctc acg ggc atc ttc atc cac cgg gtc acc ccg ggc      2009
Ile Gly Gly Asn Leu Thr Gly Ile Phe Ile His Arg Val Thr Pro Gly
                590                 595                 600

tcg gcg gcg gac cag atg gcc ttg cgc ccg ggc acc cag att gtg atg      2057
Ser Ala Ala Asp Gln Met Ala Leu Arg Pro Gly Thr Gln Ile Val Met
            605                 610                 615

gtt gat tac gaa gcc tca gag ccc ttg ttc aag gca gtc ctg gag gac      2105
Val Asp Tyr Glu Ala Ser Glu Pro Leu Phe Lys Ala Val Leu Glu Asp
        620                 625                 630

acg acc ctg gag gag gcc gtg ggg ctt ctc agg agg gtg gac ggc ttc      2153
Thr Thr Leu Glu Glu Ala Val Gly Leu Leu Arg Arg Val Asp Gly Phe
    635                 640                 645
```

Fig. 1C

```
tgc tgc ctg tct gtg aag gtc aac acg gac ggt tat aag agg cta ctc      2201
Cys Cys Leu Ser Val Lys Val Asn Thr Asp Gly Tyr Lys Arg Leu Leu
650                 655                 660                 665

cag gac ctg gag gcc aaa gtg gcg acc tcg ggg gac tca ttc tac atc      2249
Gln Asp Leu Glu Ala Lys Val Ala Thr Ser Gly Asp Ser Phe Tyr Ile
                670                 675                 680

cgg gtc aac ctg gcc atg gag ggc agg gcc aaa ggg gag ctg cag gtg      2297
Arg Val Asn Leu Ala Met Glu Gly Arg Ala Lys Gly Glu Leu Gln Val
            685                 690                 695

cat tgc aac gag gtc ctg cac gtc acc gac acc atg ttc cag ggc tgc      2345
His Cys Asn Glu Val Leu His Val Thr Asp Thr Met Phe Gln Gly Cys
        700                 705                 710

ggc tgc tgg cat gcc cac cgc gtg aac tct tac acc atg aag gat act      2393
Gly Cys Trp His Ala His Arg Val Asn Ser Tyr Thr Met Lys Asp Thr
    715                 720                 725

gcc gcg cac ggc acc atc ccc aac tac tcc agg gct cag cag cag ctc      2441
Ala Ala His Gly Thr Ile Pro Asn Tyr Ser Arg Ala Gln Gln Gln Leu
730                 735                 740                 745

ata gcc ctc atc cag gac atg act cag cag tgc acc gtg acc cgc aag      2489
Ile Ala Leu Ile Gln Asp Met Thr Gln Gln Cys Thr Val Thr Arg Lys
                750                 755                 760

cca tct tct ggg gga cca cag aag ctg gtc cgc atc gtc agt atg gac      2537
Pro Ser Ser Gly Gly Pro Gln Lys Leu Val Arg Ile Val Ser Met Asp
            765                 770                 775

aaa gcc aag gcc agc cct ctg cgt ttg tcc ttt gac agg ggc cag ttg      2585
Lys Ala Lys Ala Ser Pro Leu Arg Leu Ser Phe Asp Arg Gly Gln Leu
        780                 785                 790

gac ccc agc agg atg gag ggc tcc agc acg tgc ttc tgg gcc gag agc      2633
Asp Pro Ser Arg Met Glu Gly Ser Ser Thr Cys Phe Trp Ala Glu Ser
    795                 800                 805

tgc ctc acc ctg gtg ccc tat acc ctg gtg tgg ccc cat cga ccc gcc      2681
Cys Leu Thr Leu Val Pro Tyr Thr Leu Val Trp Pro His Arg Pro Ala
810                 815                 820                 825

cgg ccc cgg cct gtg ctc ctc gtg ccc agg gcg gtt ggg aag atc ctg      2729
Arg Pro Arg Pro Val Leu Leu Val Pro Arg Ala Val Gly Lys Ile Leu
                830                 835                 840

agc gag aaa ctg tgc ctc ctc caa ggg ttt aag aag tgc ctg gca gag      2777
Ser Glu Lys Leu Cys Leu Leu Gln Gly Phe Lys Lys Cys Leu Ala Glu
            845                 850                 855

tac ttg agc cag gag gag tat gag gcc tgg agc cag aga ggg gac atc      2825
Tyr Leu Ser Gln Glu Glu Tyr Glu Ala Trp Ser Gln Arg Gly Asp Ile
        860                 865                 870
```

Fig. 1D

```
atc cag gag gga gag gtg tcc ggg ggc cgc tgc tgg gtg acc cgc cat     2873
Ile Gln Glu Gly Glu Val Ser Gly Gly Arg Cys Trp Val Thr Arg His
    875                 880                 885

gct gtg gag tcc ctc atg gaa aag aac acc cat gcc ctc ctg gac gtc     2921
Ala Val Glu Ser Leu Met Glu Lys Asn Thr His Ala Leu Leu Asp Val
890                 895                 900                 905

cag ctg gac agt gtc tgc acc ctg cac agg atg gac atc ttc ccc atc     2969
Gln Leu Asp Ser Val Cys Thr Leu His Arg Met Asp Ile Phe Pro Ile
                910                 915                 920

gtc atc cac gtc tct gtc aac gag aag atg gca aag aag ctc aag aag     3017
Val Ile His Val Ser Val Asn Glu Lys Met Ala Lys Lys Leu Lys Lys
            925                 930                 935

ggc cta cag cgg ttg ggc acc tca gag gag cag ctc ctg gag gct gcg     3065
Gly Leu Gln Arg Leu Gly Thr Ser Glu Glu Gln Leu Leu Glu Ala Ala
        940                 945                 950

agg cag gag gag gga gac ctg gac cgg gcg ccc tgt cta tac agc agc     3113
Arg Gln Glu Glu Gly Asp Leu Asp Arg Ala Pro Cys Leu Tyr Ser Ser
    955                 960                 965

ctg gct cct gac ggc tgg agc gac ctg gac ggc ctg ctc agc tgt gtc     3161
Leu Ala Pro Asp Gly Trp Ser Asp Leu Asp Gly Leu Leu Ser Cys Val
970                 975                 980                 985

cgc cag gcc atc gcc gac gag cag aag aag gtg gtg tgg acg gag cag     3209
Arg Gln Ala Ile Ala Asp Glu Gln Lys Lys Val Val Trp Thr Glu Gln
                990                 995                1000

agc ccc cga tga tgcaccgtgc cccttcccgg gactgtgggg gcttctgtgt         3261
Ser Pro Arg  *


gcctgttaat gcagtcctgt tcctcagccc aggccctctt ggcacagctg tgggctcctt   3321
ggcacatgag gccggctctc cccactggct ggggtctaac cttgaaccct caccacgtgc   3381
aggtcacaca cagtgaagcc acttgtaact gcacactttt ctgtggaaac atcttcaccc   3441
tttaccaggc ttggcatggt ctgaactgga aaccctgaga atgtttctgc agtaggacag   3501
gagggacatc ttcccatgcc ttccctagaa ccggaggccc cggacttctc tggaaaaccg   3561
cctgtctgca ggcccgattc aaatctatgg gggctgcact tccctttac attttgatgt    3621
gtcaaaggct tttggagtga ccaaaagcac agaggcagcg ggtggggcgc ctgggtggtc   3681
cccaaggtcg ctgccaccct tgcccggggc agaggcataa gcccacatat gctgtgacgc   3741
tggccacctt ttctcagctt ctgaggctgc gatgcctcag gaactccagt ttacagagac   3801
cagtgtgttt acttgtaaat aaagcctctg ggtggtggag acggtacttt cagtgggtct   3861
gtgccccgtg gcccctgtgc ctgttcggtg ggggtgtccc agagaagcct ggcaccagta   3921
cccccgtcaa                                                          3931
```

Fig. 1E

```
 M   G   E   L   C   R   R   D   S   A   L   T   A   L   D   E   E   T   L   W     20
ATG GGG GAA CTG TGC CGC AGG GAC TCC GCA CTC ACG GCA CTG GAC GAG GAG ACA CTG TGG    60

 E   M   M   E   S   H   R   H   R   I   V   R   C   I   C   P   S   R   L   T     40
GAG ATG ATG GAG AGC CAC CGC CAC AGG ATC GTA CGC TGC ATC TGC CCC AGC CGC CTC ACC   120

 P   Y   L   R   Q   A   K   V   L   C   Q   L   D   E   E   E   V   L   H   S     60
CCC TAC CTG CGC CAG GCC AAG GTG CTG TGC CAG CTG GAC GAG GAG GAG GTG CTG CAC AGC   180

 P   R   L   T   N   S   A   M   R   A   G   H   L   L   D   L   L   K   T   R     80
CCC CGG CTC ACC AAC AGC GCC ATG CGG GCC GGG CAC TTG CTG GAT TTG CTG AAG ACT CGA   240

 G   K   N   G   A   I   A   F   L   E   S   L   K   F   H   N   P   D   V   Y    100
GGG AAG AAC GGG GCC ATC GCC TTC CTG GAG AGC CTG AAG TTC CAC AAC CCT GAC GTC TAC   300

 T   L   V   T   G   L   Q   P   D   V   D   F   S   N   F   S   G   E   S   S    120
ACC CTG GTC ACC GGG CTG CAG CCT GAT GTT GAC TTC AGT AAC TTT AGC GGT GAG AGC TCC   360

 D   F   D   G   L   A   G   T   S   R   N   L   R   L   L   V   T   P   G   L    140
GAC TTT GAC GGT TTG GCA GGC ACT TCT AGG AAC CTC AGG CTC CTG GTA ACC CCA GGT CTC   420

 M   E   T   S   K   L   T   E   C   L   A   G   A   I   G   S   L   Q   E   E    160
ATG GAG ACA TCC AAG CTG ACC GAG TGC CTG GCT GGG GCC ATC GGC AGC CTG CAG GAG GAG   480

 L   N   Q   E   K   G   Q   K   E   V   L   L   R   R   C   Q   Q   L   Q   E    180
CTG AAC CAG GAA AAG GGG CAG AAG GAG GTG CTG CTG CGG CGG TGC CAG CAG CTG CAG GAG   540

 H   L   G   L   A   E   T   R   A   E   G   L   H   Q   L   E   A   D   H   S    200
CAC CTG GGC CTG GCC GAG ACC CGT GCC GAG GGC CTG CAC CAG CTG GAG GCT GAC CAC AGC   600

 R   M   K   R   E   V   S   A   H   F   H   E   V   L   R   L   K   D   E   M    220
CGC ATG AAG CGT GAG GTT AGC GCA CAC TTC CAT GAG GTG CTG AGG CTG AAG GAC GAG ATG   660

 L   S   L   S   L   H   Y   S   N   A   L   Q   E   K   E   L   A   A   S   R    240
CTC AGC CTC TCG CTG CAC TAT AGC AAT GCG CTG CAG GAG AAG GAG CTG GCC GCC TCA CGC   720

 C   R   S   L   Q   E   E   L   Y   L   L   K   Q   E   L   Q   R   A   N   M    260
TGC CGC AGC CTG CAG GAG GAG CTG TAT CTA CTG AAG CAG GAG CTG CAG CGA GCC AAC ATG   780

 V   S   S   C   E   L   E   L   Q   E   Q   S   L   R   T   A   S   D   Q   E    280
GTT TCC TCC TGT GAG CTG GAA TTG CAA GAG CAG TCC CTG AGG ACA GCC AGC GAC CAG GAG   840

 S   G   D   E   E   L   N   R   L   K   E   E   N   E   K   L   R   S   L   T    300
TCC GGG GAT GAG GAG CTG AAC CGC CTG AAG GAG GAG AAT GAG AAA CTG CGC TCG CTG ACT   900

 F   S   L   A   E   K   D   I   L   E   Q   S   L   D   E   A   R   G   S   R    320
TTC AGC CTG GCG GAG AAG GAC ATT CTG GAG CAG AGC CTG GAC GAG GCG CGG GGG AGC CGA   960

 Q   E   L   V   E   R   I   H   S   L   R   E   R   A   V   A   A   E   R   Q    340
CAG GAG CTG GTG GAG CGC ATC CAC TCG CTG CGG GAG CGG GCC GTG GCT GCC GAG AGG CAG  1020

 R   E   Q   A   R   P   S   E   L   L   S   F   T   V   H   V   S   H   S   V    360
CGA GAG CAG GCC AGA CCC TCA GAG CTG CTG AGC TTC ACG GTC CAT GTG TCC CAC TCT GTC  1080

 Q   Y   W   E   E   K   E   Q   T   L   L   Q   F   Q   K   S   K   M   A   C    380
CAG TAC TGG GAA GAG AAG GAA CAG ACC CTG CTG CAG TTC CAG AAG AGT AAG ATG GCC TGC  1140

 Q   L   Y   R   E   K   V   N   A   L   Q   A   Q   V   C   E   L   Q   K   E    400
CAA CTC TAC AGG GAG AAG GTG AAT GCG CTG CAG GCC CAG GTG TGC GAG CTG CAG AAG GAG  1200

 R   D   Q   A   Y   S   A   R   D   S   A   Q   R   E   I   S   Q   S   L   V    420
CGA GAC CAG GCG TAC TCC GCG AGG GAC AGT GCT CAG AGG GAG ATT TCC CAG AGC CTG GTG  1260

 E   K   D   S   L   R   R   Q   V   F   E   L   T   D   Q   V   C   E   L   R    440
GAG AAG GAC TCC CTC CGC AGG CAG GTG TTC GAG CTG ACG GAC CAG GTC TGC GAG CTG CGC  1320

 T   Q   L   R   Q   L   Q   A   E   P   P   G   V   L   K   Q   E   A   R   T    460
ACA CAG CTT CGC CAG CTG CAG GCA GAG CCT CCG GGT GTG CTC AAG CAG GAA GCC AGG ACC  1380
```

Fig-2A

```
 R   E   P   C   P   R   E   K   Q   R   L   V   R   M   H   A   I   C   P   R   480
AGG GAG CCC TGT CCA CGG GAG AAG CAG CGG CTG GTG CGG ATG CAT GCC ATC TGC CCC AGA  1440

 D   D   S   D   C   S   L   V   S   S   T   E   S   Q   L   L   S   D   L   S   500
GAC GAC AGC GAC TGC AGC CTC GTC AGC TCC ACA GAG TCT CAG CTC TTG TCG GAC CTG AGT  1500

 A   T   S   S   R   E   L   V   D   S   F   R   S   S   S   P   A   P   P   S   520
GCC ACG TCC AGC CGC GAG CTG GTG GAC AGC TTC CGC TCC AGC AGC CCC GCG CCC CCC AGC  1560

 Q   Q   S   L   Y   K   R   V   A   E   D   F   G   E   E   P   W   S   F   S   540
CAG CAG TCC CTG TAC AAG CGG GTG GCC GAG GAC TTC GGG GAA GAA CCC TGG TCT TTC AGC  1620

 S   C   L   E   I   P   E   G   D   P   G   A   L   P   G   A   K   A   G   D   560
AGC TGC CTG GAG ATC CCG GAG GGA GAC CCG GGA GCC CTG CCG GGA GCT AAG GCA GGC GAC  1680

 P   H   L   D   Y   E   L   L   D   T   A   D   L   P   Q   L   E   S   S   L   580
CCA CAC CTG GAT TAT GAG CTC CTA GAC ACG GCA GAC CTT CCG CAG CTG GAA AGC AGC CTG  1740

 Q   P   V   S   P   G   R   L   D   V   S   E   S   A   Q   A   G   R   L   P   600
CAG CCA GTC TCC CCT GGA AGG CTT GAT GTC TCG GAG AGT GCA CAA GCC GGT CGT CTC CCG  1800

 A   C   S   G   V   L   M   R   R   R   P   A   R   R   I   L   S   Q   V   T   620
GCC TGC AGC GGC GTC CTC ATG CGG CGG AGG CCA GCC CGC AGG ATC CTG AGC CAG GTC ACC  1860

 M   L   A   F   Q   G   D   A   L   L   E   Q   I   S   V   I   G   G   N   L   640
ATG CTG GCG TTC CAG GGG GAT GCA TTG CTG GAG CAG ATC AGC GTC ATC GGC GGG AAC CTC  1920

 T   G   I   F   I   H   R   V   T   P   G   S   A   A   D   Q   M   A   L   R   660
ACG GGC ATC TTC ATC CAC CGG GTC ACC CCG GGC TCG GCG GCG GAC CAG ATG GCC TTG CGC  1980

 P   G   T   Q   I   V   M   V   D   Y   E   A   S   E   P   L   F   K   A   V   680
CCG GGC ACC CAG ATT GTG ATG GTT GAT TAC GAA GCC TCA GAG CCC TTG TTC AAG GCA GTC  2040

 L   E   D   T   T   L   E   E   A   V   G   L   L   R   R   V   D   G   F   C   700
CTG GAG GAC ACG ACC CTG GAG GAG GCC GTG GGG CTT CTC AGG AGG GTG GAC GGC TTC TGG  2100

 C   L   S   V   K   V   N   T   D   G   Y   K   R   L   L   Q   D   L   E   A   720
TGC CTG TCT GTG AAG GTC AAC ACG GAC GGT TAT AAG AGG CTA CTC CAG GAC CTG GAG GCC  2160

 K   V   A   T   S   G   D   S   F   Y   I   R   V   N   L   A   M   E   G   R   740
AAA GTG GCG ACC TCG GGG GAC TCA TTC TAC ATC CGG GTC AAC CTG GCC ATG GAG GGC AGG  2220

 A   K   G   E   L   Q   V   H   C   N   E   V   L   H   V   T   D   T   M   F   760
GCC AAA GGG GAG CTG CAG GTG CAT TGC AAC GAG GTC CTG CAC GTC ACC GAC ACC ATG TTC  2280

 Q   G   C   G   C   W   H   A   H   R   V   N   S   Y   T   M   K   D   T   A   780
CAG GGC TGC GGC TGC TGG CAT GCC CAC CGC GTG AAC TCT TAC ACC ATG AAG GAT ACT GCC  2340

 A   H   G   T   I   P   N   Y   S   R   A   Q   Q   Q   L   I   A   L   I   Q   800
GCG CAC GGC ACC ATC CCC AAC TAC TCC AGG GCT CAG CAG CAG CTC ATA GCC CTC ATC CAG  2400

 D   M   T   Q   Q   C   T   V   T   R   K   P   S   S   G   G   P   Q   K   L   820
GAC ATG ACT CAG CAG TGC ACC GTG ACC CGC AAG CCA TCT TCT GGG GGA CCA CAG AAG CTG  2460

 V   R   I   V   S   M   D   K   A   K   A   S   P   L   R   L   S   F   D   R   840
GTC CGC ATC GTC AGT ATG GAC AAA GCC AAG GCC AGC CCT CTG CGT TTG TCC TTT GAC AGG  2520

 G   Q   L   D   P   S   R   M   E   G   S   S   T   C   F   W   A   E   S   C   860
GGC CAG TTG GAC CCC AGC AGG ATG GAG GGC TCC AGC ACG TGC TTC TGG GCC GAG AGC TGC  2580

 L   T   L   V   P   Y   T   L   V   R   P   H   R   P   A   R   P   R   P   V   880
CTC ACC CTG GTG CCC TAT ACC CTG GTG CGG CCC CAT CGA CCC GCC CGG CCC CGG CCT GTG  2640

 L   L   V   P   R   A   V   G   K   I   L   S   E   K   L   C   L   L   Q   G   900
CTC CTC GTG CCC AGG GCG GTT GGG AAG ATC CTG AGC GAG AAA CTG TGC CTC CTC CAA GGG  2700

 F   K   K   C   L   A   E   Y   L   S   Q   E   E   Y   E   A   W   S   Q   R   920
TTT AAG AAG TGC CTG GCA GAG TAC TTG AGC CAG GAG GAG TAT GAG GCC TGG AGC CAG AGA  2760

 G   D   I   I   Q   E   G   E   V   S   G   G   R   C   W   V   T   R   H   A   940
GGG GAC ATC ATC CAG GAG GGA GAG GTG TCC GGG GGC CGC TGC TGG GTG ACC CGC CAT GCT  2820
```

Fig. 2B

```
 V   E   S   L   M   E   K   N   T   H   A   L   L   D   V   Q   L   D   S   V    960
GTG GAG TCC CTC ATG GAA AAG AAC ACC CAT GCC CTC CTG GAC GTC CAG CTG GAC AGT GTC  2880

 C   T   L   H   R   M   D   I   F   P   I   V   I   H   V   S   V   N   E   K    980
TGC ACC CTG CAC AGG ATG GAC ATC TTC CCC ATC GTC ATC CAC GTC TCT GTC AAC GAG AAG  2940

 M   A   K   K   L   K   K   G   L   Q   R   L   G   T   S   E   E   Q   L   L   1000
ATG GCA AAG AAG CTC AAG AAG GGC CTA CAG CGG TTG GGC ACC TCA GAG GAG CAG CTC CTG  3000

 E   A   A   R   Q   E   E   G   D   L   D   R   A   P   C   L   Y   S   S   L   1020
GAG GCT GCG AGG CAG GAG GAG GGA GAC CTG GAC CGG GCG CCC TGT CTA TAC AGC AGC CTG  3060

 A   P   D   G   W   S   D   L   D   G   L   L   S   C   V   R   Q   A   I   A   1040
GCT CCT GAC GGC TGG AGC GAC CTG GAC GGC CTG CTC AGC TGT GTC CGC CAG GCC ATC GCC  3120

 D   E   Q   K   K   V   Q   R   R   R   H   P   R   I   N   P   S   Q   R   T   1060
GAC GAG CAG AAG AAG GTG CAA CGC CGA CGT CAT CCA AGA ATT AAC CCA AGC CAG AGG ACG  3180

 G   I   A   T   Q   Q   R   Q   C   H   R   R   I   N   P   R   Q   R   M   G   1080
GGC ATC GCC ACC CAG CAA CGC CAG TGT CAC CGA AGA ATT AAC CCA AGG CAG AGG ATG GGC  3240

 I   A   T   Q   Q   R   Q   C   H   R   R   I   N   P   S   Q   R   T   G   I   1100
ATT GCC ACC CAG CAA CGC CAG TGT CAC CGA AGA ATT AAC CCA AGC CAG AGG ACG GGC ATC  3300

 T   T   Q   Q   C   Q   C   H   R   R   I   N   P   S   Q   R   T   G   I   A   1120
ACC ACC CAG CAA TGC CAG TGT CAC CGA AGA ATT AAC CCA AGC CAG AGG ACG GGC ATC GCC  3360

 M   P   S   S   S   D   T   L   K   K   D   K   L   L   P   R   N   T   T       1139
ATG CCT TCA TCT TCG GAC ACT CTC AAA AAA GAT AAG CTT CTG CCC AGA AAC ACC ACA      3417
```

Fig. 2C

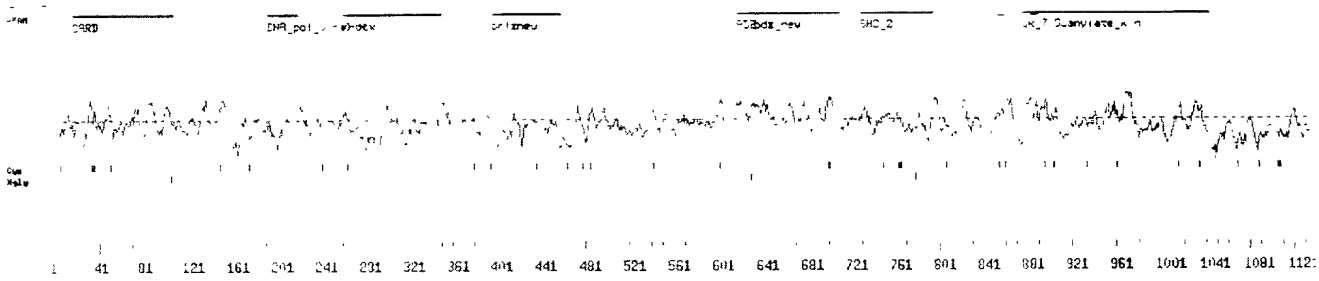
CRD
1
41
81
121
161
201
241
281
321
361
401
441
481
521
561
601
641
681
721
761
801
841
881
921
961
1001
1041
1081

Fig.3

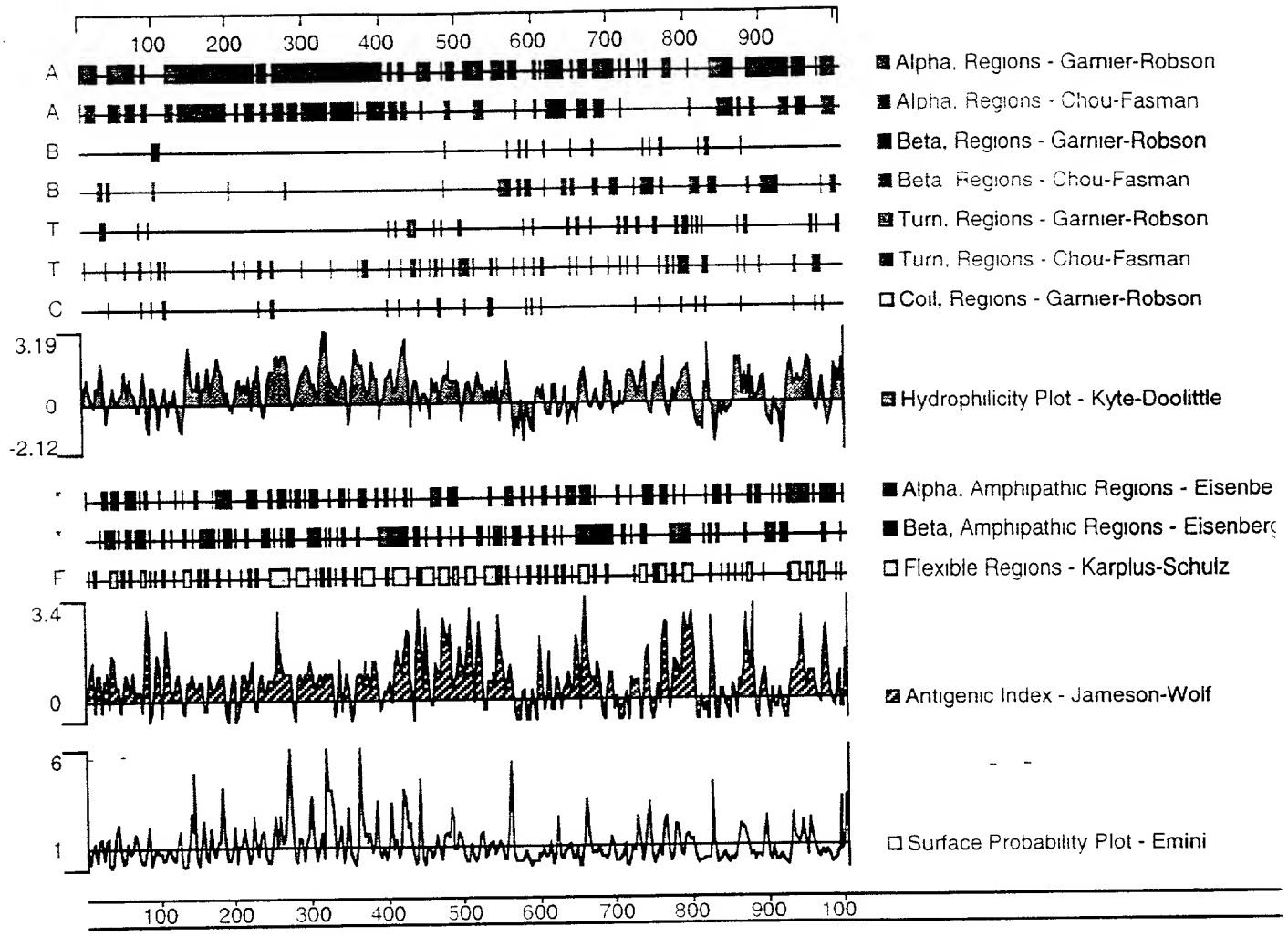
100
200
300
400
500
600
700
800
900
A
A
B
B
T
T
C
Alpha, Regions - Garnier-Robson
Alpha, Regions - Chou-Fasman
Beta, Regions - Garnier-Robson
Beta Regions - Chou-Fasman
Turn, Regions - Garnier-Robson
Turn, Regions - Chou-Fasman
Coil, Regions - Garnier-Robson
3.19
0
-2.12
Hydrophilicity Plot - Kyte-Doolittle
Alpha, Amphipathic Regions - Eisenbe
Beta, Amphipathic Regions - Eisenberg
F
Flexible Regions - Karplus-Schulz
3.4
0
Antigenic Index - Jameson-Wolf
6
1
Surface Probability Plot - Emini
100
200
300
400
500
600
700
800
900
100

Fig. 4

```
CARD: domain 1 of 1, from 16 to 107: score -4.1, E = 0.94
                 *->aeddrrllrknrlellgeltlsglLdhLleknvLteeeeEkikaknt
                    +e    +  + +r + +  +++s l  +L++++vL + +eE++   +
      CARD14    16    EETLWEMMESHRHRIVRCICPSRLTPYLRQAKVLCQLDEEEVLHSPR 62

                    trr..dkareLiDsvqkkGnqAfqiFlqaLretdqelladlllde<-*
                     + +  +a  L+D ++++G + + +Fl++L+  +++ +  +   +
      CARD14    63 LTNsaMRAGHLLDLLKTRGKNGAIAFLESLKFHNPDVYTLVTGLQ    107
```

Fig. 5A

Docket No. P0500

```
PDZ: domain 1 of 1, from 568 to 659: score 5.3, E = 0.39
                     *->eitlekevkrgglGfsikggsdk..givvsevlpGsgaAeagGrLke
                        ++t+    ++  l  +i++ + + +gi++ +v pG +aA++   L++
          CARD14   568    QVTMLAF-QGDALLEQISVIGGNltGIFIHRVTPG-SAADQMA-LRP 611

                     GDvIlsvNG........qdvenmsheravlaikgsgg..evtLtvlRd<-
                     G +I+ v+ + +++  +  +e+ ++e+av +++   g   ++++v  d
          CARD14   612 GTQIVMVDYeaseplfkAVLEDTTLEEAVGLLRRVDGfcCLSVKVNTD   659

                     *

          CARD14     -   -
```

Fig. 5B

```
SH3_2: domain 1 of 1, from 679 to 744: score -4.5, E = 3.8
                    *->eyvvAlYDyeaqnedELsFkkGDiitvleks..ddgWweGelnr...
                       +y ++  + e++  +EL ++ +++++v++   ++ g w + + ++ +
      CARD14    679    FYIRVNLAMEGRAKGELQVHCNEVLHVTDTMfqGCGCWHAHRVNsyt 725

                    ...tGkeGlfPsnYVeeie<-*
                     ++t   G +P    + ++
      CARD14    726 mkdTAAHGTIPNYSRAQQQ    744
```

Fig. 5C

```
Guanylate_kin: domain 1 of 1, from 856 to 948: score -24.2, E = 0.073
                   *->TRpVpRpgEvdGkdYhFVssrEemekdIaaneFlEygefqgnyYGTs
                                        +++s  Ee e+  ++++ +  ge++g     +
      CARD14   856    --A------------EYLS-QEEYEAWSQRGDIIQEGEVSGGRCWVT 887

                   letvrqvakqgKiciLDvepQgvkrlrtaelsNPivvFIaPpSl..qele
                   +++v+   +++ +++LDv ++ v  l   +   Piv+ +    +  + l+
      CARD14   888 RHAVESLMEKNTHALLDVQLDSVCTLHRMDIF-PIVIHVSVNEKmaKKLK 936

                   krLegrnkesEes<-*
                   k L+++++ sEe+
      CARD14   937 KGLQRLGT-SEEQ    948
```

Fig. 5D

```
K-box: domain 1 of 1, from 239 to 325: score -36.5, E = 2.9
                    *->dsyqkssgnss..lwesnyqnwqqEaaKLkaqienLQnNrnqRhllG
                        s+ ++++  ++   +s++++  +E+++Lk+++e+L+  +
      CARD14    239     VSSCELELQEQslRTASDQESGDEELNRLKEENEKLR--SL------ 277

                    EdLgsLslKELqqLEqqLEkgLkhIRsrKnqllldqieelqkKErelqee
                        + sl E   LEq L+++    R  + + l++ i+ l+ +  + + +
      CARD14    278 ----TFSLAEKDILEQSLDEA----RGSRQE-LVERIHSLRERAVAAERQ 318

                    NkaLrkKiee<-*
                     +   + +ee
      CARD14    319 RE---QYWEE    325
```

Fig. 5E

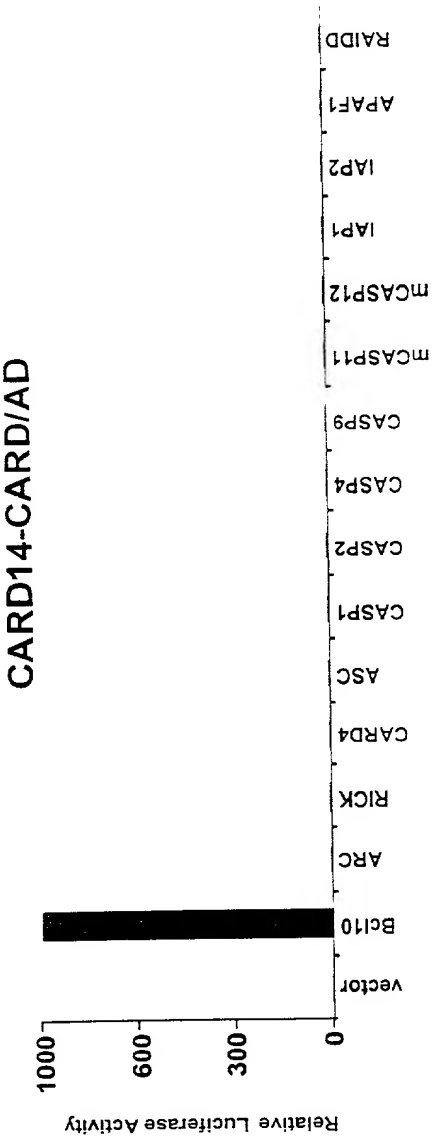
CARD14-CARD/AD
Relative Luciferase Activity
1000
600
300
0
vector
Bcl10
ARC
RICK
CARD4
ASC
CASP1
CASP2
CASP4
CASP9
mCASP11
mCASP12
IAP1
IAP2
APAF1
RAIDD

Fig. 6

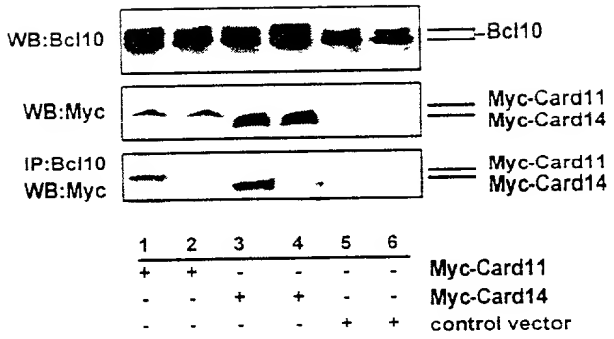
WB:Bcl10
Bcl10
WB:Myc
Myc-Card11
Myc-Card14
IP:Bcl10
WB:Myc
Myc-Card11
Myc-Card14
1 2 3 4 5 6
+ + - - - - Myc-Card11
- - + + - - Myc-Card14
- - - - + + control vector

Fig. 7

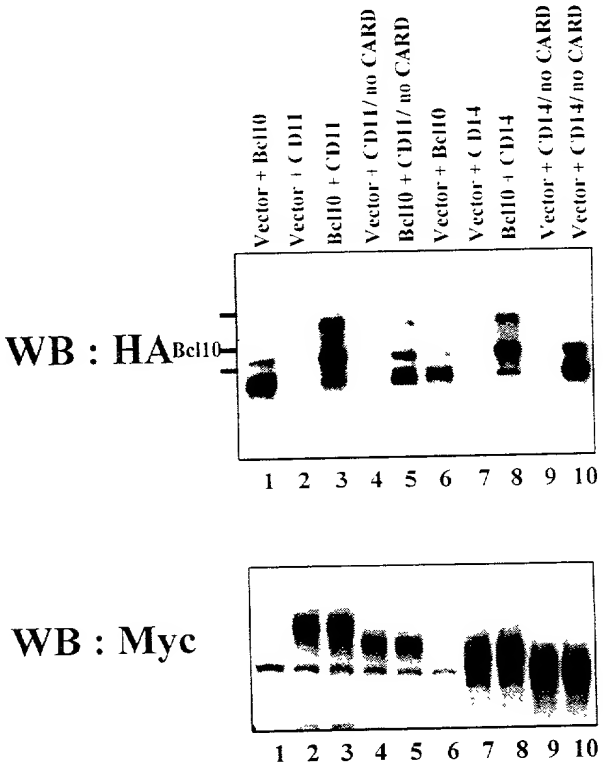
Vector + Bcl10
Vector + CD11
Bcl10 + CD11
Vector + CD11/ no CARD
Bcl10 + CD11/ no CARD
Vector + Bcl10
Vector + CD14
Bcl10 + CD14
Vector + CD14/ no CARD
Vector + CD14/ no CARD
WB : HABcl10
1 2 3 4 5 6 7 8 9 10
WB : Myc
1 2 3 4 5 6 7 8 9 10

Fig. 8

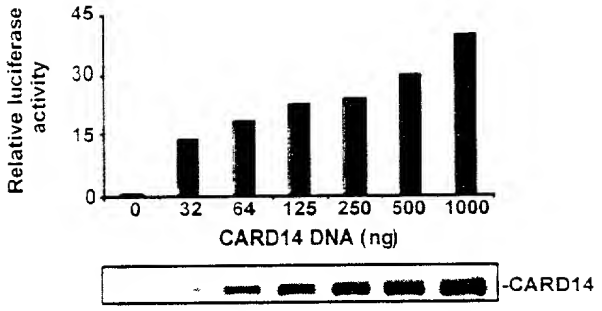

Fig. 9A

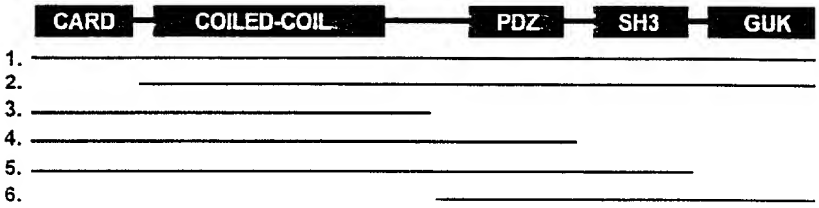

Fig. 9B

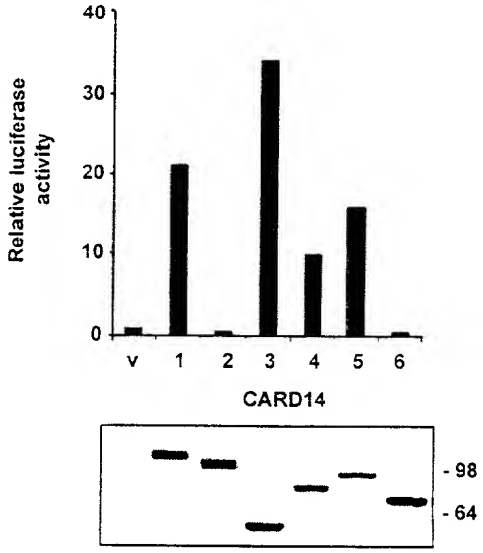

Fig. 9C